

APPENDIX A

PROPOSED COUNT FOR INTERFERENCE

Count 1:

A humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from human acceptor immunoglobulin heavy and light chains, which humanized immunoglobulin specifically binds to an antigen with:

- (i) an effective antigen binding activity, or
- (ii) an affinity constant of at least 10^7 M^{-1} and no greater than about four-fold that of the donor immunoglobulin,

wherein said humanized immunoglobulin comprises amino acids from the donor immunoglobulin framework outside:

- (a) the Kabat and Chothia CDRs, or
- (b) both the Kabat CDRs and the structural loop CDRs of the variable regions,

wherein the donor amino acids replace corresponding amino acids in the acceptor immunoglobulin heavy or light chain frameworks, and each of said donor amino acids:

- (I) is adjacent to a CDR in the donor immunoglobulin sequence, or
- (II) (a) contains an atom within a distance of 4 of or (b) is spatially close to a CDR in said humanized immunoglobulin .